for teaching of a method of identifying biological samples, and Porter et al, is cited for a teaching of whole frame imaging by bright field illumination and confocal image collection to reduce photobleaching. For at least the following reasons, Applicants traverse the rejection.

It is asserted in the Office Action that Walt et al. teaches a population of microspheres immobilized at random positions on a substrate at page 22, lines 9-22. Applicants respectfully disagree. When read in context, Walt et al. at page 22, lines 3-22, teaches a method of populating discrete wells in fiber cores by dripping a solution of microspheres over the fiber ends, sonicating the fibers to settle the microspheres in the wells, evaporating the solvent, and then treating the microspheres in the wells with a solution of Nafion. See, in particular, page 22, lines 10-15, for example, line 12, which states: "...sonicating the bundle to settle the microspheres into the wells.", and lines 13-15, which state: "Microspheres 10 may then be fixed into the wells 250 by using a dilute solution of sulfonated Nafion..." Walt et al. does mention random distribution of beads (see abstract and page 6, lines 5-6), but requires that the "random distribution" be "on a patterned surface" (page 6, line 6), resulting in patterned immobilization. In contrast, Applicants claim microspheres immobilized at random on a substrate.

Porter et al. does not overcome the deficiency of Walt et al. The Office Action indicates Porter et al. is referenced for its teaching of bright field illumination (*see* page 9 of Office Action). However, a reference must be considered for all it teaches. Porter et al. is directed to patterned immobilization of a target on a patterned surface for use as a height referencing biochemical cassette. Porter et al. requires the three-dimensional patterning in order to be effective in determining bonding of target molecules. See, for example, page 2, lines 28-31; page 3, lines 4-6; and page 5, lines 18-50. Porter et al. does not disclose or suggest random immobilization on a substrate, and does not overcome the deficiency of Walt et al.

As noted in Applicants' Amendment mailed July 2, 2004, and as discussed herein, both Walt et al. and Porter et al. teach patterning of microspheres on a substrate for ease of identification of targets on imaging. As discussed above, Walt et al. teaches and exemplifies microspheres patterned on a substrate to form a two- or three-dimensional configuration. See, for example, the abstract; page 6, lines 2-4 ("... the use of a substrate comprising a patterned

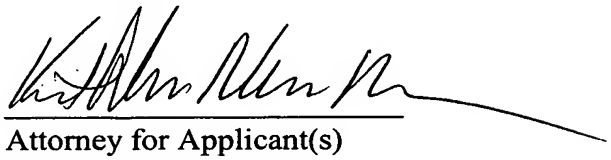
surface..."); page 7, lines 14-18 (two-and three-dimensional configurations); page 7, lines 27, through page 8, line 5 (patterning of microsphere sites); page 8, lines 7-8 (patterning in wells); page 8, lines 21-23 ("... the surface of the substrate is modified to contain chemically modified sites, that can be used to attach, ... the microspheres of the invention to the discrete sites or locations of the substrate."); page 22, lines 3-22 (placing microspheres in wells on fibers); page 22, lines 30-32 (adding slurry of beads to surface with attachment sites); page 23, lines 17-20 (adding solution of beads to surface with wells); and page 25, lines 1-4 (non-random chemical attachment). As stated herein, Walt et al. does mention random distribution of beads (see abstract and page 6, lines 5-6), but requires that the "random distribution" be "on a patterned surface" (page 6, line 6). Walt et al. thus does not teach random immobilization as required by Applicants' claims, only random distribution of beads to a patterned area where the beads are immobilized in a set pattern. Porter et al. requires three-dimensional patterning in a height-referencing cassette for detection and determination of bound molecules. See, for example, page 3, lines 4-6, and page 4, lines 63-66. Taken together, one of ordinary skill in the art would presume that some form of two-or three-dimensional patterned immobilization would be necessary in imaging and detection of the microspheres, as taught by both Walt et al and Porter et al. One skilled in the art would not expect successful detection from random immobilization techniques when all detection techniques taught in Walt et al. and Porter et al. rely on discretely patterned immobilization of the subject to be detected.

For at least the above reasons, Applicants submit the combination of Walt et al. with Porter et al. does not disclose or suggest the subject matter of the claimed invention, and in fact teaches away from the claimed invention, because both references teach the need for discretely patterned immobilization of the subject matter to be detected, in contrast to the random immobilization of microspheres claimed by Applicants. Review of Walt et al. and Porter et al. provides no motivation to randomly immobilize microspheres as set forth in Applicants' claims 21-25, because both references teach the importance of patterned immobilization for ease of identification of targets on imaging.
For at least the above reasons, reconsideration and withdrawal of the rejection is in order, and is respectfully requested.

For at least the reasons set forth above, Applicants submit all of Claims 1-25 are in condition for allowance. Prompt and favorable action in the form of a Notice of Allowance is respectfully requested.

Should the Examiner require anything further, or have any questions, the Examiner is asked to contact Applicants' undersigned representative.

Respectfully submitted,



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